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THE RELATIONSHIP BETWEEN AIR LEAD AND BLOOD LEAD IN CHILDREN: A CRITICAL REVIEW

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ABSTRACT

A review is given of community studies from which the relationship between air lead and blood lead in children of varying ages can be estimated. The review covers nineteen different studies which were carried out in ten different countries.

The blood lead/air lead relationship is denoted with the symbol 'α'. It is concluded that for children, a wide range of α-values can be estimated from the data in the different studies. Most values center on 3–5 rather than the 1–2 which is usually reported for adults. However, adjustment for confounders has been absent or incomplete in most, if not all studies. Most α-estimates thus have to be viewed with caution.

INTRODUCTION

For a variety of reasons, young children are considered to be the population at risk for lead [1]. Children are exposed to lead in food, drinking water, air, housedust, streetdirt, soil and other media [2]. Internationally, regulation of lead in the environment has concentrated on specifying air quality criteria or standards. Thus, it is important to consider the relationship between air lead and blood lead in children, and to consider also whether air lead can represent lead in other media as well, or whether these other media have to be taken into account separately. The next section will discuss the relevant scientific issues concerning the complicated problem of lead uptake from the environment by children. A detailed examination will then be given of community studies which can be used to estimate quantitatively the relationship between air lead and blood lead in children.

SCIENTIFIC ISSUES

Mouthing behaviour. The normal child will put inedible objects and its hands into the mouth relatively frequently, during some period largely confined to the preschool ages of 1–6 [3–7]. Thus, young children who live and play in a polluted environment have an additional route of exposure that does not operate at all, or to a lesser extent, in older children and adults. Specific attention paid to non-air sources of lead is necessary when studying these children.

Curvilinearity of blood lead/lead exposure relationship. Several reports in the literature indicate that the relationship between lead exposure and blood

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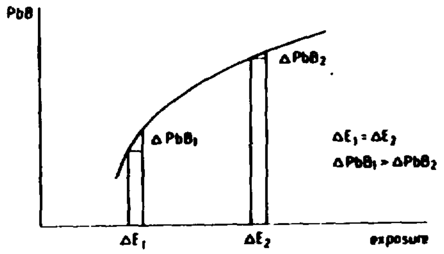

Fig. 1. Curvilinear dependence of blood lead on lead exposure.

lead is curvilinear and concave downward [8–13]. Although it has been suggested that departure from linearity is not great at PbB levels below 30 μg/100 ml [12], it is prudent to specify the PbB range to which a given blood lead/lead exposure relationship applies. At higher levels of PbB, shallower slopes are expected than at lower levels of PbB (cf. Fig. 1). Mathematically, this can be expressed in (a.o.) a log–log relationship irrespective of whether, for any particular data set, a linear or even concave upward relationship would give a better statistical fit.

Blood sampling and analysis. Proper analysis of lead in blood requires uncontaminated blood samples, skill and experience [14,15]. The taking of capillary (as opposed to venous) blood samples has repeatedly been shown to result in a systematic upward error of PbB values [8, 15–17]. As a consequence, direct comparison of the results of "capillary" studies with the results of "venous" studies is not advisable. Past and present interlaboratory studies have shown the difficulty of obtaining correct, or at least comparable results when equal samples are analysed by different laboratories [18,19]. Rigid quality control is necessary and published study results should include some reference to the employed quality control procedures and results.

When this requirement is not fulfilled, it cannot simply be assumed that the blood lead analyses have been "bad", as editors of different scientific journals do not seem to use uniform criteria with regard to this point. A rough classification, however, would separate studies with no published quality control data from those with published quality control data but without participation in some established interlaboratory quality control programme, and both of these from studies where the blood lead analyses have been carried out within some established interlaboratory quality control programme.

Environmental sampling and analysis. Although quality control problems exist here as well [18], interlaboratory programmes have been less customary and quality control data are usually not published. Classification of studies with respect to quality control is thus not possible. To some extent, this is probably justified by the concentrations which are higher in several environmental media than in blood and/or by the matrices which are usually simpler than blood. The result, however, is that standardization of sampling methods in particular has not received much attention. Only outdoor air has been sampled in most studies by High Volume samplers (although other types of samplers are also used relatively frequently), but the location of the samplers with respect to proximity to highways, industries and street level varies widely, if reported at all. Still, it is well known that concentration levels of lead in air vary significantly in close proximity to (busy) roads and lead-emitting industries, and also vary with elevation above street level [20–23]. Consequently, reported lead concentrations in outdoor air have different but usually unestimable relationships to the "true" personal exposure of the target population in different studies. This issue is further complicated by the fact that most people (including young children) spend only a limited part of their time outdoors [24,25]. It has been shown that the outdoor lead concentration is only poorly correlated to personal lead exposure [26]. Personal air lead exposure has never been measured in children, however, and studies with air sampling inside the homes of the complete study population are rare (cf. Review section below).

Indoor/outdoor comparisons for lead in air have consistently shown that indoors, the lead concentration in air is lower [17, 27–30]. It is conceivable that the long-term average personal exposure is overestimated by using outdoor air concentrations as measures of exposure, especially around industrial sources of lead where lead in air has been shown to be more concentrated in larger particles than in urban aerosol [31–33]. The larger particles which to a certain extent are co-sampled by Hi-Vol samplers [34] penetrate less well into buildings than small particles [30], thus the indoor/outdoor ratio of air lead is probably smaller in these situations than in urban situations with a traffic-generated lead aerosol mostly in the submicron range. Although this is matter of speculation because of the lack of specific data in the literature, blood lead/air lead slopes derived from "smelter" studies might not be valid for general urban conditions for this reason alone.

Apart from air, other environmental samples that have more or less regularly been taken include: lead in dustfall, usually measured as the sum of dry and wet depostion; lead in soil, where a variety of sampling methods, sampling depths and extraction methods make results of different studies difficult to compare; lead in street dust and dirt, where the difference in sampled grain sizes, especially, makes comparison between studies difficult; lead in housedust, sampled by wiping floors, windowsills etc. by tissues or gauzes, by emptying the local vacuum cleaner or by sampling standardized surfaces in a standard manner with a filter-equipped vacuum cleaner.

An attempt has been made to reconcile a number of studies from which relationships between blood lead and lead in soil, dirt and/or housedust can be derived [35, 36]. The differences between these studies in measuring exposure were not taken into account, and might explain part of the variability of the results.

The issue of environmental exposure is further complicated by the lack of steady-state in many of the studied situations.

The accumulation of lead in soil through industrial emissions is probably more related to total past emission than to actual emission, especially when counteractive measures are being, or have been taken [37–39]. For instance, the lead content of petrol has varied in the past, lead has been introduced into petrol in different countries at different times, variations of petrol lead content and traffic density may not have been parallel in different countries. Consequently, lead concentrations in different environmental media can be only moderately correlated, although coming from the same source [8,40]. Environmental exposure in such situations cannot simply be characterized by the lead concentration in one medium like air, dustfall or soil.

The estimation of the impact of a specific source or source category on blood lead levels in children by statistical analysis of the relationship between blood lead and environmental lead is thus made difficult, at best. The difficulties can partly be overcome by labelling lead from a specific source or source category as was done in the Turin isotopic lead experiment [41–43] which will be discussed further (see Discussion section).

Confounding. In epidemiology, being a largely observational, non-experimental science, the issue of confounding has received much attention [44]. A confounder is a variable related to both the dependent variable (blood lead in this case) and the independent variable(s) (environmental lead in this case), leading to an upward or downward distortion of the "true" relationship between dependent and independent variable(s).

In the case of the relationship between air lead and blood lead, there are many possible confounders. In the context of this article, all lead to which children can be exposed, but which does not come from the sources which bring lead into the air (vehicular traffic and lead-emitting industries), is considered to be a possible confounder of the relationship between air lead and blood lead.

As such, lead originating from paint on wooden structures, street kerbs and bridges can be considered [45–48]. Lead is also present in food, from which probably most of the lead uptake occurs in children not living in heavily polluted environments [1,2,49]. Lead can be present in drinking water, when lead pipes and/or storage tanks are in use [50–54]. A number of social factors has been shown to be related to elevated blood lead levels in children, like low educational level and/or income of parents, hispanic or black ethnic, lack of parental care, substandard housing conditions, low dietary calcium, impoverished play environment, etc. [55–63]. These factors too can act as confounders when covarying with environmental lead exposure. As elevated exposure and unfavourable social conditions often are both concentrated in old city centres, the problem of disentangling the different influences upon blood lead levels is not an easy one to solve.

Statistical analysis. Ideally, all possible confounders should be taken into account when deriving a blood lead/air lead relationship from a community study. This can be achieved by comparing blood lead concentrations between groups which differ only in exposure to lead in air and in other environmental media, in so far as these have been polluted by the same source. It will be clear from the onset that it is not easy to find groups which are equal in all of the many different possible confounders. Another possibility is to perform some multivariate statistical analysis in which an adjustment is made for some or all of the confounders before calculating the blood lead/air lead relationship. This requires information on the value of each confounder for each individual, a requirement that has proved to be too difficult to meet in virtually all studies performed in the past. As already mentioned, in the case of lead several confounders tend to work in the same direction as air lead. When adjustment is incomplete, the relationship between air lead and blood lead will probably be inflated.

In principle, adjustment for confounders is necessary, even when in some specific situation some of them are not correlated with blood lead in a statistically significant fashion [64–65]. As has been noted in the case of lead effects on the central nervous system [66], adjustment usually implies that all of the shared variance between confounder(s) and exposure variable(s) is attributed to the confounder, which inevitably leads to underestimation of the "true" impact of the exposure variable, when expressed as percentage of "explained" variance of the outcome variable. The situation is further complicated when more than one environmental exposure variable is entered into the analysis. Adjusting for environmental exposures which may very well be determined to a large extent by the same environmental source leads to underestimation of the true impact of environmental lead on blood lead. The concentration of lead in air cannot be manipulated as such, but only by influencing the sources which bring lead into the air, and into other environmental pathways. Adjusting the blood lead/air lead slope for these other environmental pathways thus simply does not make sense unless one can prove, for a specific situation, that lead in pathways like dust and dirt originates mainly from other sources than lead in air.

The already-mentioned possibility of poorly correlated pollution concentrations in different media polluted by the same source adds extra confusion.

To prevent overconservative estimates of blood lead/environmental lead relationships, it would seem prudent to have the environment represented by one exposure variable at a time, whilst acknowledging that the proper exposure variable will vary from situation to situation. Also, presentation of both unadjusted and (stepwise) adjusted relationships is advisable, to allow insight in the range of possible values for the relationship. As will be shown in the next section, however, adjustment for confounding factors has been absent or incomplete in the majority of published studies.

REVIEW OF STUDIES ON THE RELATIONSHIP BETWEEN AIR LEAD AND BLOOD LEAD IN CHILDREN

Some characteristics of the reviewed studies are given in Table 1. Information is presented about the type of environment studied, i.e., "urban/suburban" with mainly traffic as a pollution source, or "industrial" with smelters, battery factories, etc. as sources (in view of the earlier mentioned difference between "urban" and "industrial" sources, "industrial" studies will be discussed first, and "urban" studies second). Next, the number of children studied according to age are shown. Type of blood sampling (venous/capillary) and presence of quality control data follow. The method of air

TABLE 1

CHARACTERISTICS OF STUDIES ON THE RELATIONSHIP BETWEEN AIR LEAD AND BLOOD LEAD IN CHILDREN

No	Reference	Description of study	Population	Blood sampling	Quality control data	Air sampling	Other environmental samples	Covariates*	Statistical model	PbB (µg/100 ml)
1	Cavalleri et al (1981) [67]	Industrial	3–6 n = 110 6–11 n = 143 School populations, living close to or at > 4 km from a lead smelter	Venous	Yes, an interlab comparison	Hi Vol(?)		3, 18	Group comparisons	15.8 (3–6, g.m., exposed) 16.1 (6–11, g.m., exposed) 8.2 (3–6, g.m., control) 7.8 (6–11, g.m., control)
2	Brockhaus et al (1976) Rosmanith et al (1976a, b, 1979) [69–71]	Urban/industrial	2–14 n = 404 (industrial) 2–14 n = 606 (urban)	Not given	Reference to small interlaboratory study	Not given	Lead deposition	3, 7	Group comparisons	12.6–40.4 (a.m.) industrial, depending on season; 7.8–12.5 (a.m.) urban, depending on selection
3	Kraine et al (1977) Zielhuis et al (1979) Brunekreef et al (1981) Diemel et al (1981) [76–79]	Industrial	2–3 n = 198 (1976) 1–7 n = 680 (1977) 1–3 n = 96 (1978) Volunteers (1976), all children in area invited (1977, 1978), participation rate > 80%	Venous	Yes, no information about participation in interlab study	Hi Vol	(only in 1978) Dustfall, soil street dirt, indoor air, indoor deposition, floor dust	3, 13, 18 (1976) 3, 18 (1977) 3, 4, 5, 10, 13, 15, 17, 18, 19 (1978)	Group comparisons (1976, 1977) multiple regression, single log (1978)	11.8–19.7 (g.m.) depending on area (1976) 14.0–20.7 (g.m.) depending on area (1977) 16.1 (g.m.) (1978)
4	Landrigan et al (1976, 1981) Morse et al (1979) [32, 37, 81]	Industrial	1–18 n = 259 (exposed) 1972 n = 498 (control) n = 148 (exposed) 1977	Venous	No	Hi Vol	Dust fall and house dust	3, 4, 5, 12, 13	Group comparison	17.7–41.4 depending on area and year of sampling
5	Popovac et al (1982) [83]	Industrial	1–> 15 n = 68 (exposed) n = 73 (control)	Venous	No, small inter-laboratory study reported	Method not given		3	Group comparison	6.8–10.0 (a.m., controls) 35.2–46.8 (a.m., exposed)
6	Prpić-Majić et al (1983) [36]	Industrial	0–15 n = 379 (exposed) 1978 0–15 n = 30 (control) 10–12 n = 38 (exposed) 1979 School age n = 64 (exposed) 1982	Not given	No, reference to 2 international quality control programmes	Not given		3, 18	Group comparison	31.2–62.3 (a.m.) exposed, depending on age and year of sampling 10.3–10.8 (a.m.) control
7	Roberts et al (1974a, b, 1975) [31, 83, 84]	Urban/industrial	0–10 n = 1128 (exposed) 0–14 n = not given (control)	Capillary	No	Hi Vol	Soil, dustfall, vegetation, indoor air	14	Group comparison	27.0–28.0 (a.m.) exposed 19.0 (a.m., assumed) unexposed
8	Roels et al (1976, 1978, 1980) [86–87]	Industrial/urban/rural	10–15 n = 214 (exposed) 1974–1978 combined 10–12 n = 148 intermediate 10–12 n = 223 rural 10–14 n = 65 urban	Venous	Yes, national and international inter-laboratory programme	Low volume	Hand dust, playground dirt, dustfall	3, 4, 14	Group comparison multiple regression	26.0–30.1 (a.m.) exposed 13.3–21.1 (a.m.) intermediate 8.8–10.7 (a.m.) control 10.4–12.7 (a.m., urban) control depending on year of sampling
9	Schmitt et al (1979) Neri et al (1978) [88, 89]	Industrial	1–6 n = 200 exposed 13–14 n = 141 exposed 1–6 n = 151 control 13–14 n = 103 control	Not given	Yes	Not given	Soil	3	Group comparisons	11–22 (a.m., exposed) 10–14 (a.m., control)
10	Wagner et al (1981) [90]	Industrial	10–15 n = 98 exposed n = 61 control	Venous	No	Not given		–	Group comparisons	31.6 (a.m., exposed female) 30.7 (a.m., exposed male) 19.1 (a.m., control female) 21.0 (a.m., control male)
11	Yankel et al (1977) [40] Walter et al (1980) [92] Snee (1982) [94]	Industrial	1–9 n = 1149 (1974) n = 781 (1975)	Venous	No	Hi Vol	Soil, house dust	3, 4, 12, 13, 14, 19	Group comparisons/multiple regression single log	18–77 (g.m., 1974) 22–61 (g.m., 1975) depending on age and exposure category
12	Angle et al (1979, 1974) [8, 96]	Urban/suburban/industrial	1–6 urban/suburban n = 242 6–18 urban/suburban/industrial n = 832, Volunteers	Capillary	No	Hi Vol	Dustfall, soil, house dust	1, 3, 4, 5	Multiple regression, log–log covariates not included	21.6 (all, g.m.) 23.9 (1–5, g.m.) 22.3 (6–10, g.m.)
13	Bérode et al (1980) [99]	Urban/suburban	6–10 n = 287 Random sample	Venous	Yes, including small interlaboratory study	Method not given		2, 3, 4, 5, 7, 8, 9, 14, 15, 16, 17	Group comparisons	12.8 (all, g.m.)
14	Billick et al (1979, 1980, 1983) [50, 72, 73]	Urban	0–> 6 n = 178 533 Presented for screening	Venous	Yes, participation in CDC blood lead proficiency testing programme	Hi Vol		1, 3, 7, 18	Multiple regression with geometric group means as dependent variable	17.2–30.4 (g.m.) depending on age, race and year
15	Brunekreef et al (1983) [100]	Urban/suburban	4–6 n = 195 Nursery school populations, living in city centre or in suburban area	Venous	Yes, international quality control programme	Low volume	Dustfall, deposition indoors, soil street dirt, floor dust, hand dust	2, 3, 4, 6, 10, 11, 12, 13, 14, 15, 16, 17, 18	Group comparisons and multiple regression using log-log transformations	7.9–13.1 (g.m.) depending on area
16	Johnson et al (1975, 1976) [105/106]	Urban/rural	1–16 n = 38 (urban) n = 46 (suburban)	Venous	Yes	Hi Vol	Soil	1, 3, 8, 4, 13	Group comparisons	Male 20.8, female 14.9 (urban, g.m.) male 10.4, female 9.6 (rural, g.m.)
17	Johnson et al (1978) [17]	Urban	1–9 n = 52 (male) n = 64 (female)	Mostly capillary, some venous	Yes, including inter-laboratory study	Hi Vol	House dust, soil, indoor air	1, 3, 4, 8, 12, 13, 15, 17, 18	Group comparisons/multiple regression	Male 15.4 (g.m.) female 16.7 (g.m.)
18	Rosmanith et al (1977a, b) [112, 113]	Urban	2–14 n = 413	Not given						5.0–7.6 (a.m.) urban, second study
19	Okubo et al (1979) [114] Okubo et al (1983) [115]	Urban/suburban	6–18 n = 1033 (1976–1980)	Not given	Yes	Not given		3	Group comparisons	4.5–18.1 (g.m., exposed, depending on age and sex) 3.8–7.6 (g.m., control, depending on age and sex)

(continued)

No	α_1	α_2	Comment
1	3.3		For 2–6 years olds
	4.0		For 8–11 years olds
2	1.1		
	3.0		
	7.2		Depending on season
	2.0		
3	4.0	3.6	Adjusted for parental education
	3.6		All estimates for 2–3 years olds
4	3.7		Air lead differences estimated
	2.0		
5	1.7		0–2 years olds
	1.6		2–5 years olds
	1.6		5–10 year olds
	1.6		10–15 year olds
	1.1		> 15 year olds
6	1.8		Preschool children
	1.9		School children
	20.7		Calculated under non steady state conditions, for school children
	1.0		School children, based on decline
7	4–4.5		Children PbB in control group assumed equal to average PbB of adults and children combined
8	4.1–7.4		Calculated over large PbA range
	2.9–3.8		Calculated over small PbA range at high PbA level
	0.3–31.2		Calculated over small PbA range at low PbA level
	5.3		Regression analysis on all data
9	0.3		For 1–6 years olds
	0.7		For grade 9 children (13–14 year olds)
10	12.5		For girls
	17.7		For boys
11		1–1.4	Calculated in [110] after adjustment for soil lead
	2.4–3.3		Calculated from 1974 data, group comparisons, depending on age
		1–2.5	Calculated in [109] after adjustment for soil lead
12	0.06	–	
	−1.60	–	From regression coefficients
	2.10	0.60	
	15.0	–	Group mean comparison, all children
13	1.6–	1.5	* Estimated from incomplete data
	2.0		
14	–	3.2	Adjusted for age and race
		2.9	Also adjusted for measuring height of air lead
15	24.5		Group comparison
	10.4	8.5	Regression analysis
16	1.8		For males
	0.9		For females
17	–		No significant relationship between air lead and blood lead
	–		
18	4.5		Estimated from incomplete data
19	> 10		Time lag not taken into account

[a]Covariates: 1, race, 2, nationality, 3, age, 4, drinking water, 5, food; 6, milk consumption/calcium intake, 7, season, 8, traffic density/proximity to roadways; 9, population density, 10, age of home, 11, crowding/number of rooms, 12, paint status of home, 13, parental education, 14, parental job attainment/income, 15, mouthing behaviour/hand dirtiness, 16, presence of pets, 17 exposure through parents' occupation or hobbies, 18, geographic area, 19, house dustiness

sampling and some information on other environmental samples, covariates and the applied statistical model are also given. Mean PbB levels and estimates of the blood lead/air lead slope (α_1 = unadjusted; α_2 = adjusted) conclude the table. The α estimates were calculated for the $0.5 - 1.5\,\mu g/m^3$ air Pb range, as the most relevant level for urban areas, in those instances where curvilinear relationships were given. The studies are evaluated in this section in the same order as they appear in the Table.

First study. Cavalleri et al. [67] studied 253 children of nursery and primary school age, living in the surroundings of a lead smelter. The smelter underwent emission reduction prior to the study, and as a consequence the problem of a delayed effect on PbB due to persisting lead in the surrounding environment was present here. Exposed and control groups of both age categories showed a large difference in PbB values.

Air lead was sampled close to the smelter (150–300 m) and in the control area. The average values were 2.9 and $0.6\,\mu g/m^3$, respectively. Based on group mean differences in PbB of 7.7 and 9.1 $\mu g/100$ ml, respectively, and an air lead difference of $2.3\,\mu g/m^3$, α_1 values of 3.3 and 4.0 can be calculated.

No information was given on any possible confounder, which means that the results have to be interpreted with care.

As a result of the emission reduction prior to the study, the α_1's may have been overestimated as the PbB values in the exposed groups could be the result of persisting lead in soil, housedust, etc. However, air lead was sampled very close to the source (150–300 m), and as it is well known that air lead values decline rapidly within short distances from smelters, the values reported may have been overestimates of the actual exposures encountered by the children. No information was given on the exact location of schools and homes of the exposed children.

Second study. A complicated study was carried out in 1973/1974 in a heavily contaminated industrial area in Nordrhein–Westfalen, West Germany [68–71]. The yearly average air lead concentration in this area was reported to be $5.6\,\mu g/m^3$, and extreme lead deposition values of $500 - > 10.000\,\mu g/m^2$ per day were found. In a control area an average air lead value of 1.1 $\mu g/m^3$ was found.

In the exposed area the PbB of 404 randomly chosen children was measured in March and May 1973, and an average PbB of $16.7\,\mu g/100$ ml was reported; 29 additional children volunteered to have their PbB determined in May 1973, and their blood lead averaged $21.9\,\mu g/100$ ml. This was interpreted by the authors as evidence of a selection effect on PbB values. However, when the March and May results for the first group were reported separately, a large difference became evident (average PbB 12.6 and $21.2\,\mu g/100$ ml, respectively). A seasonal influence rather than a selection effect would seem to be present in the data. Some children had their blood lead level determined again in August and October, and the results were even more striking: 40.4 $\mu g/100$ ml in August, and $20.9\,\mu g/100$ ml in October. Analytical procedures were checked and were not found to be responsible. Thus, an extreme seasonality was present in these data which was attributed by the authors to outdoor play in spring and summer. Increases were largest in the 4–5 year olds who had the highest blood lead levels in May. The seasonality in this study is much more extreme than the seasonality noted in some U.S. studies [72–74]. In the recent E.C. survey of 1981 in the U.K., no difference between children's blood lead levels in samples taken in March, April and May was found [75]. The Einbrodt/Rosmanith study thus stands alone, but cannot be dismissed as invalid in view of the extreme exposure conditions that existed. In the control area 393 children were sampled at random, and 293 presented themselves voluntarily for blood lead analysis. All samples were taken in December 1973 and January 1974, and the "random" results (7.8 $\mu g/100$ ml) were clearly lower than the "voluntary" results (12.5 $\mu g/100$ ml). In the control group, a selection effect cannot be explained away.

α_1 estimates based on the "random" results from both areas and based on an air lead difference of 4.5 $\mu g/m^3$ would give different results for different seasons: 1.1 in March, 3.0 in May 7.2 in August and 2.9 in October. If, in heavily contaminated areas, fluctuations of PbB as large as noted in this study do occur, exact knowledge about the date of blood sampling is required to facilitate interpretation.

Third study. The surroundings of a secondary lead smelter located in Arnhem, The Netherlands, have been investigated repeatedly in the period 1976–1978 [76–79]. The smelter has been in operation since World War II, and emissions were restricted during the 'seventies, for the last time in 1977, i.e., in the midst of the investigations.

Venous blood samples were taken from 108 (1976), 690 (1977) and 95 (1978) children, respectively. The results for the 2–3 year olds are shown in Table 2, according to distance from the smelter. This age category was chosen for comparison, being the only category sampled in each year. In 1976 and 1978, blood lead analyses were performed by the same laboratory. In 1977, another laboratory did the analyses.

Air lead was measured at 6 sites during the 1978 study and was found to be uniformly low (0.3–0.5 $\mu g/m^3$). In 1977, air lead varied between 0.4 and 1.6 $\mu g/m^3$, and in 1976 between 0.5 and 2.5 $\mu g/m^3$ [77,80]. Although measuring sites and periods have not been completely comparable through the years, an influence of the emission reduction that was enforced in the spring of 1977 can be detected in the data.

A decline of PbB also seems present in the most exposed group. For estimating α in 1976, an air lead difference of 2.0 $\mu g/m^3$ was assumed between the highest and lowest PbB group. An α_1 of 4.0 results. The PbB difference of about 8 $\mu g/100$ ml decreased to 7.2 $\mu g/100$ ml after adjustment for parental education, resulting in a slightly lower α_2 estimate (3.6). For 1977, an air lead difference of 1.0 $\mu g/m^3$ was assumed between exposed and control children of 2–3 years old and which had average values of 18.2 and 14.6 $\mu g/100$ ml, respectively. An α_1 estimate of 3.6 results. In 1978, a direct estimate of α was not possible as air lead did not correlate with PbB within the exposed population. Soil lead and lead deposition indoors were significantly associated with PbB, indicating the influence of still-present, recirculating lead in the environment.

TABLE 2
BLOOD LEAD (PbB IN $\mu g/100$ ml, n IN PARENTHESES) IN 2–3 YEAR OLDS ACCORDING TO DISTANCE FROM THE ARNHEM SMELTER

1976	400–1000 m	1000–2000 m	> 2000 m
1976	19.7 (17)	14.7 (53)	11.8 (36)
1977	18.2 (88)	14.6 (96)	–
1978	16.6 (67)	–	–

TABLE 3
REDUCTION OF ENVIRONMENTAL LEAD AND BLOOD LEAD IN EL PASO TX BETWEEN 1972 AND 1977

	1972 < 0.8 km from source	1972 0.8–1.6 km from source	1977 < 0.8 km from source	1977 0.8–1.6 km from source
PbB ($\mu g/100$ ml, arithmetic means)	41.4	31.2	17.7	20.2
Number of children studied	160	96	3	137
Mean age	8.9	9.7	13.3	9.1
Air lead ($\mu g/m^3$)	10.0	6.0 (est.)	5.5	3.0 (est.)
House dust lead (mg/kg)	22191		1479	
Soil lead (mg/kg)	1791		427	

Fourth study. A large number of children was studied in the surroundings of a lead smelter located in El Paso, TX, in 1972 [32,81]. The immediate surroundings of the smelter were extremely polluted, with annual average air lead values of 8–10 $\mu g/m^3$. The early reports from this study concentrated on specifying the percentage of children per area with PbB values above a given level (e.g., 40 $\mu g/100$ ml or 60 $\mu g/100$ ml) and did not supply sufficient information to derive quantitative relationships between environmental lead and blood lead.

In 1977, a small follow-up study was carried out to ascertain whether emission reductions which were introduced in the preceding years had been effective in reducing environmental lead and blood lead [37]. From this study, Table 3 has been compiled.

The reduction of PbB within 0.8 km of the smelter cannot be considered as being well documented, in view of the small number of children studied in this area in 1977. Between 0.8 and 1.6 km from the smelter the reduction of PbB was clear. However, air lead values for this particular area were not given and had to be obtained by interpolation of air lead values reported at 0.4 and 4 km from the source, respectively.

α_1 estimates of 2.6 (1972) and 3.7 (based on reduction of PbA and PbB at

0.8–1.6 km from the source) are thus obtained. α_1 estimates for 1977 and for the reduction of PbA and PbB within 0.8 km from the source have not been calculated in view of the extremely limited number of children who were studied in 1977 in this area. The environmental data from this study are unusual in showing a large reduction of lead levels in soil and housedust. The extremely arid climate with its accompanying wind erosion has been held responsible for this phenomenon. No statistical correction for confounders is possible on the basis of the reported data. Family income, paint lead exposure, lead in drinking water and lead release from pottery were however shown to be reasonably uncorrelated with distance from the smelter.

Fifth study. A large lead smelter located in Kosovska Mitrovica, Yugoslavia, has caused one of the gravest lead pollution problems mentioned in the literature [82]. Citywide average air lead values of 14.3 $\mu g/m^3$ and 23.8 $\mu g/m^3$ were reported for the years 1978 and 1980, respectively. PbB was measured in a control group of 73 children in 1978, and in 179 exposed children in 1980. In 1978, 107 exposed children had their PbB determined, but those children were selected for having a high FEP reading before, and cannot serve as a representative sample of exposed children.

Assuming an air lead difference of 23.5 $\mu g/m^3$ between exposed and unexposed children, α_1 can be estimated at 1.1 to 1.7, depending on age (cf. Table 1). Considering the large exposure range over which these α_1's were calculated, it is quite conceivable that their comparatively low value is at least partly related to the presumed curvilinearity of the blood lead/environmental lead relationship. The reported increase in PbA levels between 1978 and 1980 further indicates a non-steady state; it is conceivable that the PbB values which have been shown to lag behind changes in environmental exposure (cf. ref. 38) were still increasing..

Sixth study. Another heavily polluted area in Yugoslavia is the Meza Valley [38]. In the years 1974–1976, an average air lead value of 20.8 $\mu g/m^3$ was recorded without an indication of change over time. In 1978, a bag filter system was introduced and air lead values declined to 1.6–1.9 $\mu g/m^3$ over the years 1979–1982. Table 4 shows the results of blood-lead level determinations in children in different years.

A number of different α_1 estimates can be derived from these data. First, in 1976, α_1 values of 1.8 (preschool) and 1.9 (school age) can be derived for the prevailing presumed steady-state conditions. Here again, the values seem to have been forced downward in view of the large range of exposures studied. For 1979, an α_1 of 26.7 can be calculated: an obviously inflated value caused by the persistence of high PbB values despite a radical drop in PbA values. Taking the drop in PbB values of school children between 1976 and 1982, and α_1 of 1.0 is calculated. This is most probably an underestimate as it is quite likely that in the future PbB values will continue to decline as children grow up who have been born after the emission reduction of 1978, and as lead levels in house dust, street dirt and eventually top soil will decline.

An interesting comparison can be made between this study and the earlier discussed one by Morse et al. [37]. Apparently, the rate of decline of PbB

TABLE 4

PbB VALUES[a] IN CHILDREN IN THE MEZA VALLEY, YUGOSLAVIA, FOR THE YEARS 1976–1982

	1976	1979	1982
Preschool children, exposed	46.7 (30)[b]		
School children, exposed	49.2 (30)	52.3 (28)	31.2 (54)
Preschool children, control	10.3 (19)		
School children, control	10.5 (11)		
Air lead ($\mu g/m^3$), exposed	20.8	1.6	1.9
Air lead, control	0.1		

[a] PbB in $\mu g/100$ ml (arithmetic means).
[b] Number of children in parentheses.

values is more or less comparable, although the climate in North Western Yugoslavia is almost certainly less arid than in El Paso. One is led to wonder what changes in lead in soil, housedust and dustfall have occurred in the Meza Valley over the years, and how these compare with the values cited from El Paso.

Seventh study. An extensive study was carried out in 1973 in Toronto in an area near two large lead smelters and in an urban control area [31,83,84]. Air lead averaged 3.0–3.3 $\mu g/m^3$ at 100 and 60 m from one of the smelters, and 0.9 $\mu g/m^3$ in the urban control area. Within short distances of the smelters, heavy deposition of lead occurred.

Capillary blood was analyzed for lead and was found to average 27.0 and 28.0 $\mu g/100$ ml in 0–15 year old children living within 30 m of the respective smelters, and 19.0 $\mu g/100$ ml in an urban control population of similar socio-economic background. The average PbB for children in this group was not reported; it was only stated that less than 1% of 0–14-year olds in the control group had PbB > 40 $\mu g/100$ ml. When it is assumed that the average PbB of control children was 19.0 $\mu g/100$ ml as well, and when an air lead difference of 2 $\mu g/m^3$ is assumed between exposed and control children, α_1 estimates of 4 and 4.5 result.

It is clear that the use of capillary blood may have inflated these estimates; that the absence of separately reported data for control children adds uncertainty; and that the age range was too broad to cover only the age category at the highest risk.

Eighth study. A large lead smelter and its surroundings in Hoboken near Antwerp, Belgium, has been repeatedly studied between 1973 and 1978 [85–87]. Schoolchildren in the age category of 10–15 were sampled in an area located < 1 km from the smelter in the 5 consecutive years 1974–1978. An intermediately exposed group with its school at 2.5 km from the smelter was sampled during the same period.

Rural controls were sampled in 1974–1976 and 1978, urban controls in 1976 and 1978. Lead emission of the smelter was reduced in 1975 and the

TABLE 5

AIR LEAD AND BLOOD LEAD IN DIFFERENT POPULATIONS OF SCHOOL AGE CHILDREN IN BELGIUM, 1974–1978

Year	Population	Air lead ($\mu g/m^3$)	PbB (μg/100 ml, a.m.)	*n*
1974	< 1 km from smelter	4.06	30.1	37
	2.5 km from smelter	1.00	21.1	14
	Rural	0.29	9.4	92
1975	< 1 km from smelter	2.94	26.4	40
	2.5 km from smelter	0.74	13.6	29
	Rural	0.31	9.1	45
1976	< 1 km from smelter	3.67	24.6	38
	2.5 km from smelter	0.80	13.3	40
	Urban	0.45	10.4	26
	Rural	0.30	9.0	44
1977	< 1 km from smelter	3.42	28.9	56
	2.5 km from smelter	0.49	14.8	50
1978	< 1 km from smelter	2.68	27.8	43
	2.5 km from smelter	0.54	16.0	36
	Urban	0.56	12.7	29
	Rural	0.37	10.7	42

study can thus be compared to the earlier-discussed ones [37,38,76–79] in which such non-steady state conditions were also present.

Air lead was sampled by low volume methods in the different areas, and the air lead values might thus be lower than those that would have been found by high volume sampling, especially near the smelter where more of the lead will have been concentrated in the larger particles. The results of the different surveys can be summarized as follows (Table 5) [87].

A regression analysis on the combined survey data which was performed by the authors resulted in an α_1 estimate of 5.3 (5.8 for boys, 5.0 for girls). This estimate covers the whole range of PbB values encountered, and the data in Table 5 can also be used to check whether the α_1 estimates would be higher at lower levels of exposure. This was achieved by making 18 different between-group comparisons, contrasting 6 pairs with large differences in exposure, 5 pairs with small differences of exposure at high exposure levels and 7 pairs with small differences of exposure at low exposure levels. Table 6 shows the results.

The Table shows that α_1 values were clearly dependent on exposure level in these studies. The high estimate at the lower exposure level is influenced by 2 extreme values of 16.7 and 31.2; the other five values fell in the narrow range of 8.3–11.3. The authors have, on the basis of children's hand lead levels, argued that most of the lead was probably ingested and not inhaled. It is arguable whether mouthing behaviour can still be expected to be prevalent in this age category; the α_1 values however exceed those usually found in

TABLE 6

α_1 ESTIMATES FOR DIFFERENT LEVELS OF EXPOSURE FROM ROELS ET AL. STUDY

		Mean α_1 ± S.D.	Range	*n*
1.	< 1 km from smelter vs. urban/rural (extended range)	5.9 ± 1.4	4.1– 7.4	6
2.	< 1 km from smelter vs. 2.5 km from smelter (high exposure level)	4.6 ± 1.2	2.9– 5.8	5
3.	2.5 km from smelter/urban vs. urban/rural (low exposure level)	13.7 ± 8.2	8.3–31.2	7

adults (cf. Discussion section) to a large extent and a predominant route of uptake other than inhalation, be it mouthing behaviour or not, will have to be assumed.

On the basis of PbB group means for girls and boys in 4 different areas in 1978, the authors performed a multiple regression analysis with air lead and hand lead as independent variables. The analysis resulted in a significant contribution of hand lead but not of air lead to PbB after the other independent variable had been taken into account. However, air lead and hand lead were shown to be extremely well correlated in both girls and boys (r = 0.995 and 0.999, respectively).

This collinearity prevents meaningful interpretation of the multiple regression analysis and it does not seem valid to conclude from the result that the quantitative contribution of air lead to the childrens blood is negligible compared to that of hand lead. The method of air sampling underestimated air lead levels, probably especially in the most heavily exposed area, which would mean that the α_1 estimates from this study are inflated. On the other hand, one wonders what would have been found if younger age categories had been studied.

Another interesting feature of this study is that PbB levels remained elevated despite an emission reduction in 1975. However, judging from the air lead levels which were measured through the years, the reduction must have been far less efficient than the ones cited from Arnhem, El Paso, and Meza Valley.

Ninth study. Another smelter study was carried out in Trail, Canada in 1975 [88,89]. Children aged 1–6 and 13–14 (grade 9) were investigated in Trail and in Nelson, a control town. Air lead levels averaged 2.0 and 0.5 $\mu g/m^3$, respectively. In young children, PbB levels were higher in Trail (22 μg/100 ml) than in Nelson (14 μg/100 ml), a difference which was not observed in the older age group (11 vs. 10 μg/100 ml). α_1 values of 5.3 and 0.7 can be calculated for the respective age groups; the low value for the oldest age group is in especially marked contrast with the results of the Belgian study [87] which covered much the same age range. An explanation cannot easily be given. For the young children, lead in soil was shown to be closely related to PbB.

Tenth study. A smelter study from Czsechoslovakia was reported by Wagner et al. [90]. Air lead near a secondary smelter was reported to average $1.5\,\mu g/m^3$, compared to $0.5\,\mu g/m^3$ in a control area. In 1976, blood was sampled from 10–15 year old children by venous puncture, and their PbB values were found to be markedly different between exposed and control groups, especially in boys (cf. Table 1). Large α_1 estimates result from this study, depite the fact that PbB levels were high, also in the control group. Lack of published information prevents further interpretation of this study.

Eleventh study. The last industrial study to be discussed in this review is perhaps the most frequently cited in the literature: the Silver Valley Lead Study [40,91–93]. In 1974, 1149 children aged 1–9 were studied and in 1975, another 781 children age 1–10, all living at varying distances from a large lead smelter located in Kellogg, ID.

Average air lead levels close to the smelter averaged $16.7\,\mu g/m^3$ in 1974, having risen rapidly since 1971 when they were only $6.1\,\mu g/m^3$ and slightly lower than in the period 1966–1970 [91]. Contributing to the extremely high air lead levels in 1974 was a fire in a bag house within the smelter; after replacing the unit, air lead levels were lower again in 1975, averaging 10.3 $\mu g/m^3$ close to the smelter. Geometric mean PbB levels ranged from 18 to the extreme of $77\,\mu g/100$ ml, depending on age and exposure category. It *has been suggested that an upward error could have been present in the 1974* PbB data due to contamination of samples taken in the field under badly contaminated circumstances [91,92]. The 1975 survey was performed under circumstances which make comparison between the 1974 and the 1975 population samples invalid: [92] selective out-migration had occurred of children with high PbB living close to the smelter; in the lesser exposed areas, only children whose blood lead had been greater than $40\,\mu g/100$ ml in 1974 were studied again in 1975; some children with high PbB values in 1974 had subsequently been treated by chelation therapy; an extensive home hygiene campaign had taken place in the community and schools; people were more aware of the problem in 1975 than in 1974; top soil had been replaced in some badly polluted places; and emissions had been reduced.

Analysis of the data by the original investigators yielded α_2 estimates of 1–2.5, depending on exposure level. For the $0.5–1.5\,\mu g/m^3$ range, the author's equation as mentioned in [40] predicts an α_2 value of 1.1 at a soil lead level of 1000 ppm and average values for 3 modifier variables in the equation. α_1 estimates were not given. The single-log model which was used was unusual in predicting larger PbB increases at high PbA levels than at low PbA levels; adjustment for lead in soil must have led to an underestimate of the "true" impact of environmental lead on blood lead. This does not seem to have been fully appreciated by the U.S. EPA when it promulgated its ambient air quality standard for lead in 1978 [93]. The Silver Valley Lead Study was the main study used by EPA to estimate "the" blood lead/air lead slope for children, and although the selected value of 2 was motivated by, among others, some qualitative statements about the possible role of soil lead and dust lead, EPA at the time did not realize that it would have been more correct simply to calculate a blood lead/air lead slope without adjusting it for soil lead.

The data were reanalyzed by Snee [94] in an effort to provide a new estimate of the relationship between blood lead and air lead. Three different analyses were performed: group comparisons for the average data obtained in 1974 only or in 1974/1975 combined; analysis of the individual results obtained in 1974 and 1975; and comparison of the blood lead results of children sampled in both 1974 and 1975. None of these analyses is without serious problems.

In the group comparisons, the data from 2 control areas were pooled, although one control area had distinctly elevated geometric mean PbB values of $29–38\,\mu g/100$ ml, depending on age; probably due to previous lead mining activity which was reported for this area. The incorporation of this "control" area in the analysis led to an underestimate of the α_1 values. Instead of the calculated values of 0.8–1.7, values of 1.5–2.6 result when only the uncontaminated control area is incorporated in the analysis. A further underestimate was introduced by restricting the analysis to areas with air lead values below $10\,\mu g/m^3$. When the highest and lowest exposed categories are compared, α_1 values of 2.4–3.3 (depending on age) result from the 1974 data. Admittedly, this does indicate the very unusual phenomenon of a steeper rise of PbB at high levels of exposure than at low levels of exposure; a characteristic of the data which could be explained by blood lead analysis problems, as there are no studies in the literature which indicate that blood lead levels of children living near lead smelters could rise to levels anywhere near those found in 1974 in Kellogg, despite the fact that several situations have been studied where exposure conditions were as bad as or even worse than in the Silver Valley. The α_1 estimates for the combined 1974/1975 data obtained by Snee were more variable and ranged from 0.5–2.0. The same criticism holds as for the 1974 data. In view of the selection which occurred when sampling the 1975 population, I would rather prefer not to use the 1975 data at all. In the regression analysis, emphasis was put upon interpreting the partial regression coefficient of ln PbB on air lead (untransformed). This procedure was justified on two different occasions by the author by stating that there were no strong correlations between predictor variables [94,95]. The general incorrectness of this procedure has been pointed out already in the previous section. Moreover, the correlation coefficient between air lead and soil lead was 0.52 in 1974 and highly significant. As will be shown in the case of the Omaha Study, even lower correlations between independent variables are sufficient to reduce a partial regression coefficient as much as threefold [8]. Presentation of adjusted as well as unadjusted regression coefficients is the only correct procedure, which cannot be replaced by general statements. The regression analysis was of the single-log type, and performed for all subjects and for subjects with air lead $< 10\,\mu g/m^3$ separately. From the resulting equations, α_2 values were calculated for the PbA ranges $0.5–2\,\mu g/m^3$, and $2–5\,\mu g/m^3$. Due to the single-log type equation, the α values which were calculated for only the lower part

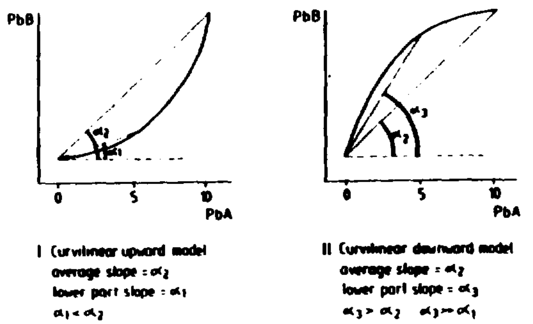

Fig. 2. Effect of model selection upon α-estimates in Silver valley lead study.

of the complete range of PbA values used to specify the relationship are lower than the average α, calculated over this complete range. The reverse result would be obtained when a curvilinear downward model had been employed, which has repeatedly been shown to be the more plausible one. Figure 2 serves to illustrate this point. Performing calculations for a greater range of PbA values than is later used for deriving α estimates leads to a higher than average α in the case of the curvilinear downward model, and to a lower than average estimate in the case of the single-log model. Model selection thus led to yet another underestimate of α.

Comparison of blood lead determinations in children sampled in 1974 and 1975 is again problematic in view of the selection which took place in 1975. The restriction to children who had elevated blood lead levels in 1974 will have introduced a regression-toward-the-mean phenomenon in this analysis [96,97]. A reduction of PbB in this group thus could have been expected, irrespective of changes in exposure. This went unnoticed by the author, and could very well be responsible for the negative intercepts he found when regressing ΔPb on ΔPbA. The many changes which took place between the 1974 and 1975 survey also do not serve to lend credibility to the α estimates which were obtained in this analysis.

Twelth study. The Omaha study [8,98] is an analysis of more than 1000 blood lead values obtained from 831 children between 1971 and 1977 in Omaha, Nebraska. Some samples were taken by venous puncture, most were capillary. On some individuals both methods were used and it was found that capillary PbB was consistently 4 μg/100 ml higher than venous PbB. All venous PbB's were subsequently corrected to capillary PbB values, a rather unusual procedure in view of the aforementioned problems with capillary blood lead analyses. The population was mostly of school age and not further subdivided by age within the two classes used (1–5, 6–18). Children came from 3 areas: suburban, mixed urban/commercial and commercial.

Some industrial lead sources were present in the commercial district. Suburban children were white, children from both other groups predominantly black, introducing a cultural and probably socio-economic bias which was not accounted for in the analysis of the data. Air was sampled on one spot within each area, and geometric mean Pb air levels in a range of 0.02–1.69 $\mu g/m^3$ were assigned to the more than 1000 PbB values for further analysis. At the same spot, lead in dustfall was measured, but after preliminary calculations it was decided not to include the values in the further analysis, because of negative results and the limited number of samples obtained. Soil was sampled near 37 homes and 20 schools within the 3 areas, and levels with a geometric mean of 227 mg/kg and a 95-percentile of 843 mg/kg were assigned to the individual PbB values on the basis of the school values, or, if present, the home values. House dust was sampled at the same sites as soil, and levels with a geometric mean of 337 mg/kg and a 95-percentile of 894 mg/kg were assigned to the PbB values, in the same way as the soil levels.

Milk and water were analysed and found to be uniformly low in lead. Food was not analysed, as the major grocery chains were equally distributed in the three areas.

The analysis of the data was mainly restricted to the influence of air lead, soil lead and house dust lead on blood lead, and is thus of limited value in view of the probable influence of the earlier-mentioned confounders like race. Interesting however is that, for these three independent variables, both univariate and multivariate regression analyses were performed after transforming both PbB and the environmental variables on the log scale. The analysis thus serves as an illustration of the curvilinear, concave downward behaviour of PbB in response to environmental variables.

Unadjusted coefficients of 0.66 (all children), −2.63 (1–5-year olds) (!) and 2.10 (6–18-year olds) were obtained for the blood lead/air lead slope in the range 0.5–1.5 $\mu g/m^3$ (cf. Table 1). The analysis also serves as an illustration of the effect of adjustment on α: by incorporating soil and house dust in the analysis, α for air lead decreased more than threefold in the 6–18-year olds (from 2.10 to 0.69), despite the fact that correlations between air and soil lead (0.37) and air and housedust lead (0.17) were only moderate. Assuming the same source for lead in air, soil and housedust, adjustment leads to underestimation of the "true" impact of environmental lead on PbB, which would make it appropriate to rely on the unadjusted rather than the adjusted value. The published study results also allow a comparison of group means for the different areas. Table 7 shows that, with air lead values only slightly different, PbB values differed markedly.

Taking the difference between "commercial" and "suburban" as a lead, α_1 would be 6.8/0.43 = 15.8 rather than 0.66. This difference is suspiciously large and shows that by pooling all individuals into one group, interesting differences as shown in Table 7, went unnoticed in the regression analysis. This is not to imply that an α_1 of 15.8 is realistic. The publised data only permit linking of areawide long-term average concentrations and the lack of

TABLE 7
PbB AND AIR LEAD VALUES IN THREE STUDY AREAS OF THE OMAHA STUDY

	Suburban	Mixed urban/ commercial	Commercial
Geometric mean PbB (all children, μg/100 ml)	18.0	22.0	24.8
Air lead, averaged over 1970, 1972 and 1973 ($\mu g/m^3$)	0.40	0.69	0.83
Number of individuals	110	589	132

adjustment for important confounders also precludes definite conclusions from this study.

Thirteenth study. The study reported from Lausanne, Switzerland, by Bérode et al. [99] included 287 children, aged 0–10, living in different parts of Lausanne. The study was carried out from October–December 1975. Blood was sampled by venous puncture, and extensive quality control data concerning the blood lead analysis were published. There was no concomitant environmental sampling, but air lead levels of about 2.5 $\mu g/m^3$ were said to prevail in the central urban zone.

Lead in drinking water was uniformly low (1–5 μg/l). Information concerning a number of potential confounders was gathered by means of a questionnaire (cf. Table 1). The results showed an increase of PbB values from about 11 μg/100 ml at age 1 to about 15 μg/100 ml at ages 4 and 5, and a subsequent decrease to about 11 μg/100 ml at age 10. Among others, traffic density was shown to be related to PbB. Geographic analysis yielded mean PbB levels in 5 different zones ranging from 11.3 to 15.2 μg/100 ml. When it is assumed that the maximum between area difference in air lead is 2–2.5 $\mu g/m^3$, an unadjusted slope (α_1) of 1.5–2.0 can be calculated from these figures. Adjustment for father's profession and mouthing behaviour probably would not change this estimate to any great extent, as can be deduced from the fact that the influence of traffic density upon PbB remained largely unaffected by adjustment for these two factors The unavailability of actual air lead data within the areas of interest in the months proceding blood sampling makes the α estimates from this study uncertain.

Fourteenth study. The studies published by Billick et al. [59,72,73] cover the extremely large number of over 175 000 venous blood samples obtained from New York children mostly in the age range of 0–6 years of age, over the years 1970–1976.

PbB depended on age and race, with the highest values in black children of 2–4 years of age. Interestingly, the highest PbB values in white children occurred at age 5. There was a clear seasonal influence, and an overall decline of PbB values between 1970 and 1976.

There was no clear dependence of PbB on geographic area for blacks, and

a dependence of PbB on area for hispanics that decreased over the years. Air lead was sampled at an elevated site over the years, and the resulting air lead values were incorporated in a multiple regression analysis with quarterly geometric mean PbB as dependent variable and age and race as other independents. A highly significant correlation with air lead was established, with an (adjusted) regression coefficient of 5.16. Subsequent analyses showed an even higher dependence of PbB on petrol lead consumption, suggesting vehicular traffic as an important source of lead in the blood of these children [72]. Later, the analysis was extended to Chicago [73] and again the same pattern arose, giving further support for the conclusions reached.

Some comments, however, can be made. Air lead was measured at an elevated site, and a later comparison showed that, at the same site, air lead levels at street level were about 45% higher [20]. Adjustment for this difference thus would reduce the α estimate to about 2.9. By taking quarterly geometric mean blood lead levels as a dependent variable, any factor that varies seasonally, like blood lead, will correlate well with blood lead. Seasonal variation of blood lead levels in children has been noted before [74] and has been ascribed to other causes like sunlight, increased exposure to outdoor pollution by playing outdoors, etc. Adjustment for these factors was not attemped, and would reduce the α estimate.

A reduction of PbB values over time in children seen in screening programmes has also been noted before [46] and has been ascribed to the concentration of early screening efforts to the presumed "worst" areas, and to increasing awareness of the public for lead paint hazards due to the accompanying publicity. In the central districts of large U.S. cities especially, elevated blood lead levels have customarily been thought to be mainly related to lead in paint [45] and lead paint hazard abatement programmes cannot be dismissed as possible causes of a reduction of childhood PbB values.

Nevertheless, the data presented by Billick et al. have also shown that irregularities in seasonal petrol lead consumption have been closely mirrored by irregularities in the seasonal variation of PbB, a phenomenon that cannot easily be accounted for by other putative causes of seasonality of PbB or of PbB decreases (cf. Discussion section).

Fifteenth study. In 1981, a study was carried out on environmental exposure and blood lead in 195 Dutch city children of nursery school age (4–6 years old) [100]. Blood samples were taken as part of the screening programme of the European Communities [101]. An extensive quality-control programme was incorporated in this screening effort [102]. Several environmental variables were measured, and many potential confounders were taken into account (cf. Table 1).

Air lead was measured by low volume sampling on one urban and one suburban spot in the Rotterdam area, and was found to be low on both (0.25 vs 0.13 $\mu g/m^3$). The use of low-volume samplers in stead of high-volume samplers may have resulted in an underestimate of lead in air [103]. Even if this bias is taken into account, the difference in air lead between the urban and suburban area was probably not larger than 0.2 $\mu g/m^3$. In the Rotterdam area, geometric mean PbB values were 13.1 (urban) and 8.2 (suburban) $\mu g/100$ ml. Unadjusted estimates for the air lead/blood lead slope based on these figures yield high values of 24.5 (from group mean comparisons) and 18.5 (from regression analysis). Multiple regression analysis was carried out to adjust for a number of confounders, and an estimate of the blood lead/air lead slope after adjustment for 6 different confounders is still as high as 8.5.

Undoubtedly, these estimates are very sensitive to slight changes in the actual air lead concentration, as they are based on a between-area air lead difference which was estimated at only $0.2 \mu g/m^3$. The analysis of the data suggested a major influence of outdoor lead deposition, which was clearly different between the urban and suburban area in this study (i.e., 643 vs. $220 \mu g/m^2$/day in Rotterdam). This seems to indicate that actual lead pollution is the cause of the between-area differences in blood lead rather than some inheritance of the past. However, it has to be mentioned that petrol lead was reduced in The Netherlands by January 1, 1978 [80] and as the distribution of traffic density will not have changed greatly since then, it is conceivable that the present differences in lead deposition and air lead mirror differences that were greater in the past, and that still exert an influence through street dirt, house dust etc. Furthermore, suburban homes were, on average, constructed as late as 1974, in areas that used to be farmland, and where any traffic-related accumulation of lead has occurred for a much shorter period of time than within the urban areas where houses were, on average, constructed in 1928 and where traffic-related lead pollution must have occurred as long a lead has been added to petrol in The Netherlands.

The low PbB levels in this study could be another partial explanation of the relatively high α estimates, in view of the curvilinearity of the blood lead/lead intake relationship. A more general discussion on urban/suburban and urban/rural differences is given later.

Sixteenth study. In September 1974, 38 children aged 1–16 years and living near the San Diego Freeway in Los Angeles, were studied and compared with 46 children of the same age, living in the desert town of Lancaster, 40 miles from Los Angeles [105,106]. Venous blood samples were taken twice, one week apart, from each participant; two different reports, including one by the investigators themselves, later declared the accuracy of the blood lead analyses from this particular study to be doubtful [17,107]. Air lead was sampled in Lancaster backyards and also 80 ft down (prevailing) winds from the San Diego Freeway, for two weeks only. Two samples from Los Angeles gave an average reading of $6.3 \mu g/m^3$ and were compared to 13 samples from Lancaster, giving an average value of 0.6 $\mu g/m^3$. No information was given on prevailing wind directions during this short sampling period, making it impossible to judge whether the high Los Angeles air lead value was representative for the long term average air lead concentration at the sampling site. The housing complex from which most volunteers for this study were recruited was reported to be located between 100 and 300 ft from the Freeway. The original report further mentions that

12 children lived more than two blocks, and some of them even more than one mile away from the Freeway. Despite this, the investigators stated in a later report that "the residences studied in Los Angeles were within 100 ft from the edge of the Freeway . . ." [17], clearly contradictory to the original report. It is well known that the concentration of lead in air decreases rapidly within short distances of busy roads [22]. Thus, there is a distinct possibility that the personal air lead exposure of Los Angeles children was significantly overestimated by using air lead values that were obtained at only 80 ft from the Freeway.

The Los Angeles population was rather uncharacteristic in that it consisted mainly of children from parents with a degree (70%), an expected finding in a U.C.L.A Married Student Housing Complex. Educational status of Lancaster parents was distinctly lower (31% with degrees) and despite the well-known relationship between socio-economic factors and children's blood lead, this was not taken into account in the analysis of the data. Length of residence was shown to be related to urinary lead, and was different between the two populations, with only 40% of Los Angeles children residing for more than 4 years at their 1974 adress vs. 78% of Lancaster children. This again was not taken into account.

The age range was broad (1–16) and in view of the limited number of children studied, only few children in the proper risk category (0–6 years of age) were incorporated. In an appendix to the original report it is shown that PbB values were higher in preschool children ($19.6 \mu g/100$ ml) than in older children ($16.4 \mu g/100$ ml) in Los Angeles but not in Lancaster. This also was not taken into account, probably because the difference was not statistically significant due to the small mumber of children involved. It was mentioned that the older children visited schools well away from the Freeway. Without doubt, their personal exposure was lower than the air lead values measured close to the Freeway. This, again, was not taken into account in any of the analyses of the data from this study. In the study area, PbB values were clearly higher in male children ($20.8 \mu g/100$ ml) than in female children ($14.9 \mu g/100$ ml). For children, this is an unusually large difference, which was not further explained. α_1 estimates based on the results of this study are different for males (1.8) and females (0.9) as a result. In view of the many uncertainties than can be detected in this study, it is somewhat disturbing that it is one of the few to be cited approvingly in 4 of the 5 reviews concerning the general air lead/blood lead relationship which appeared in recent years (cf. Discussion section).

Seventeenth study. A study of the relationship between automobile traffic and blood lead levels was carried out in Dallas in the summer of 1976 [17]. Included were 116 children aged 1–8, living in 4 areas characterized by different levels of traffic density.

Blood was sampled by fingerprick in about 2/3 of the children; in the rest venous blood was sampled. Capillary samples were stated to give more variable results; from 8 children venous and capillary samples were obtained. Capillary PbB's were higher than venous PbB's but not significantly so,

TABLE 8
RELATIONSHIP BETWEEN TRAFFIC DENSITY AND AIR LEAD, DALLAS STUDY

Site	1	2	3	4
Traffic density (cars/day)	250	8000	17000	30000
Air lead ($\mu g/m^3$)	0.67	0.89	1.07	1.54

TABLE 9
CHILDRENS BLOOD LEAD LEVELS ACCORDING TO SITE, DALLAS STUDY

Site		1	2	3	4
Blood lead	Male	12.9	16.5	11.7	15.1
($\mu g/100$ ml, g.m.)	Female	14.9	18.6	14.9	13.6

probably due to the small number of pairs and the large spread in capillary values. The investigators chose to pool venous and capillary data, to avoid data loss for the subsequent statistical analysis. Air lead was measured for a total of 152 days on 17 different sites, located 15 m downwind of the road used for classifying the traffic density of the area. The results for the four different categories of roads are shown in Table 8.

There was a clear relationship between air lead and traffic density. There was only a weak relationship between soil lead and traffic density, and no relationship between indoor air lead, housedust lead and traffic density. Samples were taken in summer in a period of high outdoor temperatures, and indoor air lead was shown to be 5–10 times lower than outdoor air lead, presumably due to air conditioning. Childrens blood lead levels per site are shown in Table 9.

No relationship between air lead (or traffic density) and blood lead is evident from these figures. Multiple regression analysis did not show a significant effect of traffic density on children's blood lead after taking a number of confounding factors into account.

It is possible that the greater analytical variability associated with capillary PbB determinations has contributed to this negative finding. It is also possible that actual personal exposure of the study children simply was not different. The extremely low indoor air lead values, and the weak or absent association between traffic density and soil lead and housedust lead lend credence to the latter explanation. There is one other study in the literature in which a very weak relationship between traffic density and children's PbB has been found [108], and another study which, on the other hand, has established a clear relationship between the two measures. Absence of air lead determinations in these studies however has led me to exclude them from further analysis within this review.

Another related study was done in London in 1980 along a road carrying 25 000 petrol-driven vehicles per day [110,111]. Air lead was measured but only at the very short distances of 2 and 5 m from the kerb, and found to be between 1.4 and 2.1 $\mu g/m^3$. Blood lead was measured in 221 nursery and junior school children who had either their school, their home or both located adjacent to the road. Exposure contrasts were thus minimized in this study, and no conclusions can be drawn concerning a PbB/PbA relationship.

Eighteenth study. Another urban study was performed in a German town with some zinc and cadmium pollution, but without specific industrial lead sources [112,113]. Children of 2–14 years were divided into three groups: close to the zinc/cadmium source ($n = 84$), intermediate ($n = 36$) and city centre ($n = 293$) where some lead pollution by traffic was stated to be present. The date of blood sampling was not given, which is strange considering the extreme seasonality of PbB values reported earlier by the same authors [68–71].

PbB values were low, averaging 5.0 $\mu g/100$ ml (industrial), 5.7 $\mu g/100$ ml (intermediate) and 7.6 $\mu g/100$ ml (urban), respectively. Air lead was reported at 0.5 $\mu g/m^3$ for the urban area, and not reported for the other 2 areas. Assuming an air lead difference of 0.4 $\mu g/m^3$ between the highest and the lowest group, an α_1 estimate of 6.5 results. For young children, all α_1 estimates from these studies would probably be higher as the age range (2–14) was broad, and as higher than average blood lead levels are usually found in the young.

Nineteenth study. In Tokyo, Japan, air lead has been measured since about 1970, and children's blood lead levels were determined in the years 1975–1980 in urban as well as suburban areas [114,115]. In the urban area, air lead was above 1 $\mu g/m^3$ until about 1972. From 1975 onwards, air lead in the urban and suburban areas has been uniformly below 0.5 $\mu g/m^3$.

Blood lead levels of children have also been declining, but interestingly, differences between urban and suburban children have persisted until long after differences in air lead have virtually ceased to exist. PbB differences remained generally above 1 $\mu g/100$ ml until 1980, despite air lead differences of only about 0.1 $\mu g/m^3$. Group comparisons would yield α_1 values generally above 10. Information on possible confounders was not presented although it was stated that paint lead is not a known problem in Japan. If indeed the differences in PbB between the urban and suburban children are indirectly caused by the historical differences in PbA, this would indicate an important time lag of over 5 years, emphasizing once more the problems associated with studying non-steady state environments.

DISCUSSION

The size of the α values

In Table 10, the calculated α values are presented according to type of study, PbB level and age of the investigated children. It is not easy to detect

TABLE 10
α VALUES ACCORDING TO TYPE OF STUDY, PbB LEVEL AND CHILDREN'S AGE

Population group	Type of study Industrial Urban	Urban
1 PbB < 20–25 μg/100 ml Age 0–9	3.3 (1)[a] 3.6–4.0 (3) 5.3 (9)	1.5–2.0 (13) 8.5 (15)
2 PbB < 20–25 μg/100 ml Age 0–9, 10+	4.0 (1)	0.7–2.1 (12) 15.8 (12) 0.9–1.8 (16) 6.5 (18) > 10 (19)
3 PbB < 20–25 μg/100 ml Age 10+	8.3–31.2 (8) 0.7 (9)	
4 PbB > 20–25 μg/100 ml Age 0–9	1.6–1.7 (5) 1.8 (6) 1.0–3.3 (11)	2.9–5.2 (14)
5 PbB > 20–25 μg/100 ml Age 0–9, 10+	1.1–7.2 (2) 2.6–3.7 (4) 1.9 (6) 4.0–4.5 (7)	
6 PbB > 20–25 μg/100 ml Age 10+	1.1–1.6 (5) 2.9–7.4 (8) 12.5–17.7 (10)	

[a]Numbers in parentheses refer to number of study in Table 1.

any pattern in the results: high α values have been found in industrial as well as urban studies, at low and at high PbB levels, and in children of all age categories between 0 and about 16. Type of blood sampling (venous or capillary) and the presence or absence of quality control data do not seem to be related to the size of the α values, either. This is not to imply that the results contradict curvilinearity or age dependency of α; within studies with one exception [40], concave downward curvilinearity was repeatedly shown [8, 85–87]. Age dependency was present in some studies [40, 88] but absent from others [38].

However, in young children and at low levels of PbB, α would seem to centre on the values 3–5 rather than on lower values. The general pattern is that levels around 1.0 are rare; that levels between 1.0 and 2.0 mainly occur at high levels of PbB and/or in the higher age categories; and that there are many studies from which high values of α (above 5) can be calculated, although over small ranges of lead in air (less than one to a few μg/m^3).

It has to be stressed that it is impossible to calculate properly adjusted α values from most of the studies. Several α estimates may have been inflated simply because of this. The adjusted α estimates still range from 1.5–8.5; lead intake through food however has in no study been directly measured,

and uncertainty thus surrounds the α_2 estimates as well. The wide range in values reflects the equally wide range in values calculated for the relationship between lead in soil or dust and lead in blood [35].

The variety of circumstances under which the studies were carried out would lead one to expect a modest amount of variation between α's derived from different studies. That the variation would be as large as is suggested by this review is surprising, and has not been noticed in recent reviews concerning the air lead/blood lead relationship [11, 12, 116–118]. All of these have tended to concentrate on specifying the relationship for adults, probably more inspired by availability of data of a partly experimental nature [119–123] than by public health significance, which is obviously low for any relationship between environmental lead and blood lead in adults, given the fact that situations which are adequate for children are more than adequate for adults, with the reverse definitely being incorrect.

For adults, α estimates of 1–2 are usually given as a conclusion to the reviews. After stressing the difficulty of deriving α for children from epidemiological studies, Chamberlain [12] proceeds to mention just the Silver Valley Lead Study, and cites the α estimates of 1.0–2.5 obtained by Walter et al. [92], with a statement that the curvilinear upward relationship in this study is "unusual" as the only comment. Hammond [11] cites only one study on children, the Johnson Southern California Study [105] and concludes from this study that "α may be higher for children than for adults, but probably by a factor of less than 2".

Jones and Stephens [118] cite the studies by Billick et al. [72] and by Johnson et al. [105], but without calculating α's from them. They also mention a study on Sydney School children by Garnys et al. [124] which was not available for incorporation in this review and from which an α of "greater than 5" (actually 7.5 according to [117]) was said to be derived, a value that earlier was considered by the British DHSS Working Party on Lead to be so large that it was only able to deem it as being "unexplained" [1]. However, it has been suggested that the taking of capillary blood samples in this study has biased the results [125].

Ratcliffe [117] cites a number of studies incorporated in this review. She mentions α estimates from only a few of them, however: 7.5, from Garnys et al. [124], remarking that it probably entails a contribution from dust fall lead; 2, from Johnson et al. [105], a study which was considered "well-matched" (cf. my specific comment); 1–2 from the Silver Valley Lead Study, without further comment; 5, from Roels et al. [87], citing the results of the multiple regression of PbB on PbA and hand Pb without further comment (cf. my specific comment); 1.5–6.8 from the Goldsmith Food Chain Study [126] which was not available to me when preparing this review, but which was also one of the four studies incorporated in the review prepared by Snee [116] who mentions that the children in this study were aged from 9 to well into their teens, and who derived an α of 2.0 from this study. This estimate was even reduced to 0.7 excluding the data from one community (Burbank), which were "not consistent with the data from the other communities". The second cited study was the one by Johnson et al. [105] from which, by exclusion of some outlying PbB values, α's of 1.4 (male) and 0.7 (female) are calculated rather than the 1.8 and 0.9 values mentioned earlier. It is further stated that the larger proportion of 2–6-year olds in the Los Angeles group (42% vs. 22% in Lancaster) probably led to an overestimate of even these low α values. None of the criticisms on the Johnson study proposed earlier in this review, and which conclude the α estimates from this study to be an underestimate rather than an overestimate, can be found in Snee's review. The Silver Valley Lead Study was also discussed; the later, more detailed analysis of this study by Snee has been mentioned and discussed already in the previous section, to which I refer.

The last study cited by Snee was the Roels et al. study from Belgium [87], from which it was only concluded that hand lead was more important than air lead on the basis of the earlier-mentioned multiple regression analysis. This was accepted at face value by Snee as well as by Ratcliffe. Not all of the studies discussed here were published already when these reviews were prepared; however they have all been uncritical toward the studies cited most, the Johnson et al. Southern California Study and the Silver Valley Lead Study. Snee has tended to propose critisims mainly on the basis of their use in further reducing α estimates. Only the reviews by Jones and Ratcliffe allow for somewhat higher estimates of α.

The (im)possibility of using air lead as an indicator of risk to children

The large range of α values mentioned in this review makes one wonder whether an air lead value can be selected at all which would provide sufficient protection for the population at risk. It would seem that the relationship of a certain air lead value (obtained according to some standardized measuring protocol) with the integrated environmental exposure through all pathways can easily be different in different situations. The differential action of factors like parental education, mouthing behaviour and calcium intake further seems to make an accurate prediction of children's blood lead from air lead levels alone unlikely. A slightly more reassuring picture emerges when one concentrates on the actual blood lead levels found at different levels of PbA in the different types of studies (cf. Table 1).

From this table it becomes clear that extreme group average PbB values have only been found around lead smelters, at both high and low air lead levels; the highest group average PbB levels in urban situations were found in the United States, where a contribution of paint lead is more likely than in Europe or Japan.

A conclusion from Table 1 would be that air lead values cannot be used as "predictors" of blood lead levels around industrial sources of lead pollution. In urban areas with traffic as the main source of lead, group average PbB values as well as long term average PbA levels show less variability than the α estimates derived from urban studies.

The data presented in Table 1 still do not allow the derivation of a "safe" air lead level, but they do suggest that further compilation of data on blood

lead, air lead and other indicators of lead pollution (like lead emission per surface unit, lead deposition and lead levels in soil and dust) in urban situations would give a better indication of which urban situations actually lead to unacceptably high blood levels in children than predictions solely based on α values obtained from whichever study one would like to select from the literature.

If one wants to avoid routine surveillance through biological monitoring of children's blood lead, because of the obvious ethical drawbacks involved, the development of a set of environmental indicators would be well advised. It is possible that the large variability of blood lead/air lead relationships obtained from smelter studies can, to a certain extent, be explained by taking these other indicators into account. If so, a uniform set of indicators could probably be used to characterize both industrial and urban situations. Studies in which all of these measures were determined are few, and to date only one attempt has been made to propose some kind of integrated lead exposure function [8] incorporating lead in air, lead in soil and lead in house dust. Data from only one study were used in forming this exposure function, however, and it would be interesting to analyze individual data on blood lead and lead exposure from different studies.

As a weak surrogate, average data from different studies can be tabulated. Table 11 shows data on air lead, dustfall, soil lead, housedust lead and blood lead obtained in 9 different studies and covering 13 different child populations of varying ages.

The small number of populations, the differences in age group studied, the differences in sampling and analysis of environmental as well as blood lead,

TABLE 11
ENVIRONMENTAL LEAD AND BLOOD LEAD IN 13 DIFFERENT CHILD POPULATIONS

Reference	Air lead ($\mu g/m^3$)	Dustfall lead ($\mu g/m^2$ day)	Soil lead (mg/kg)	Housedust (mg/kg)	Blood lead (μg/100 ml)
8	0.83	680	262	479	24.8
	0.69	220	339	300	22.0
	0.40	130	81	211	18.0
127	0.34	254	4881	1803	25.0
72	0.41	467	240	282	16.1
75	0.40	643	336	190	13.1
	0.20	220	43	70	8.2
31	10.00	8000	1791	4022	41.4
36	3.00	(3000)[a]	427	1479	20.1
101	3.30	17000	7000	2055	28.0
	0.90	750	20	845	19.0
102–104	3.50	6500	4000	(4000)[a]	27.5
39	16.00	(2000)[a]	6700	12000	66.0

[a]Numbers in parentheses estimated

TABLE 12

CORRELATION MATRICES FOR ENVIRONMENTAL LEAD AND BLOOD LEAD FOR DATA MENTIONED IN TABLE 11

	ln(air lead)	ln(dustfall lead)	ln(soil lead)	ln(housedust lead)
ln(air lead)				
ln(dustfall lead)	0.923			
ln(soil lead)	0.624	0.684		
ln(housedust lead)	0.884	0.831	0.772	
ln(blood lead)	0.857	0.717	0.722	0.907

socio-cultural differences between groups and the distinct non-normality of the data do not seem to justify calculation of an integrated lead exposure function. When all variables are (log) transformed, all between-variable correlations are high (generally > 0.70, *cf.* Table 12). Thus, due to the problem of collinearity, for statistical reasons also, a meaningful exposure function cannot be derived from these data.

Studies in which only air lead and children's blood lead have been measured are much more abundant. It is interesting to plot PbA and PbB values obtained in different studies, and to find out how the resulting relationship fits in to the range of α-values calculated in the review section.

Figures 3a and 3b show air lead and blood lead values as measured in 96 different child populations of varying ages, from different countries, from 18 different study areas. Figure 3a shows the untransformed values; a distinct curvilinearity can be seen. Figure 3b shows log-transformed values for both PbA and PbB. The R^2 value for the untransformed data (0.629) is lower than for the transformed data (0.692). The data used to compile these figures are given in Appendix I. The regression equation for the transformed data is

$$\ln \mathrm{PbB} = 2.8528 + 0.3485 \ln \mathrm{PbA}.$$

This equation predicts a PbB increase from 13.6 to 19.9 μg/100 ml, when PbA is increased from 0.5 to 1.5 μg/m³: an α of 6.3. The high PbA and PbB values in this analysis come from smelter studies or from urban U.S. studies, i.e., from situations in which the relative contribution of soil and dust lead to blood lead may be larger than in urban situations, or in which a contribution of paint lead cannot easily be ruled out. Restricting the analysis to populations with PbB less than 20 μg/100 ml ($n = 43$) reduces the regression coefficient to 0.2159 ($R^2 = 0.331$). Still, a PbB increase from 11.8 to 15.0 μg/100 ml is predicted when PbA is increased from 0.5 to 1.5 μg/m³: an α of 3.2.

Of course, one should once again realize that the inherent problems in comparing groups increase when groups from different studies, performed in different countries are incorporated in one single analysis; the analysis

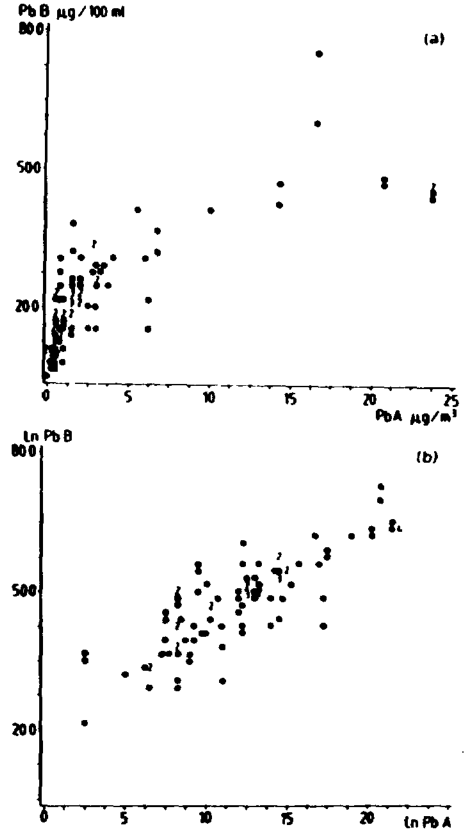

Fig. 3. Air lead and blood lead in 96 different child populations: (a) untransformed; (b) log-transformed.

merely shows that, despite the great variety of α estimates, air lead and blood lead are highly correlated when the results of a number of different studies are pooled, and it also shows that the unadjusted α estimates of 3.2 and 6.3 fit nicely within the range of α estimates obtained from analyzing each study separately.

In cancer epidemiology, worldwide group comparisons have been used to suggest an association between certain environmental or lifestyle factors (like fat consumption) and certain cancers (like breast cancer) [128]. These associations however are not interpreted as proof of a causal relationship but as indication of the existence of some manipulable factor (be it fat consumption or some covariable) which is the "real" cause.

Likewise, a "worldwide" association between air lead and blood lead does not prove a causal relationship, but can only be interpreted within the context of other available information.

It has been suggested that a log–log model overestimates α at air lead levels below 1–2 $\mu g/m^3$, because it predicts unrealistic, low baseline PbB levels at PbA levels near zero [129]. However, the aforementioned model does not produce α's for the PbA range of 0.5–1.5 $\mu g/m^3$ which are systematically higher than those obtained directly from community studies. Furthermore, at a realistic background level of 0.1 $\mu g/m^3$, a very conceivable background PbB level of 7.8 μg/100 ml is predicted, suggesting that misbehaviour of the model occurs at PbA levels well below those encountered in cities as well as rural areas in the industrialized countries.

Urban/suburban and urban/rural PbB differences

Some of the α values calculated in the Review section were based on urban/suburban or urban/rural contrasts. There are several other recent studies in which urban/suburban or urban/rural contrasts in children's PbB levels have been assessed, and it is interesting to compare them to the studies cited here.

In 1979, only small urban/suburban differences were found in West Germany; between 50-percentiles in the cities of Bremen (1 μg/100 ml), Nurnberg (1 μg/100 ml) and Bochum (2 μg/100 ml) [130]. In Amsterdam, The Netherlands, in 1979 an urban/suburban difference of 3 μg/100 ml was found [102]. In the same year, an urban/rural difference of about 5 μg/100 ml was found in the The Netherlands. In West Germany "non-exposed" rural children had PbB values which were often in excess of those in inner-city children in 1979, indicating a difference in non-air exposure which was not further clarified [130].

In the U.S., the large NHANES II survey, carried out between 1976 and 1980, revealed different PbB values in 0.5–5-year olds living in big city centres as opposed to rural areas for black (23.1 vs. 18.3 μg/100 ml) as well as white children (17.4 vs. 13.5 μg/100 ml) [60].

From Ireland, a large difference in PbB values was reported between 262 3–8-year old Dublin children (16.4 μg/100 ml) and 128 4–8-year old rural children (7.1 μg/100 ml) [131]. In Finland, however, urban/rural differences were not found in 1–5-year old children who had average PbB values well below 10 μg/100 ml [132].

For 10–12-year old children in Japan, an urban/suburban difference of 4.8 μg/100 ml (male) and 2.5 μg/100 ml (female) in PbB values has been reported [114].

From these data it becomes clear that urban/suburban and urban/rural differences vary widely in size, and are sometimes even negative. This, once again, emphasizes the complexity of the lead exposure problem.

Associations between petrol lead and blood lead

The association between petrol lead consumption and blood lead which was noted first by Billick et al. [59, 72, 73] has also been shown to be present in the NHANES II data [133–134] and other data bases [135, 136]. Although heavily disputed by representatives of industry [137, 138], the association in the NHANES II data was found to be valid by an independent panel of biostatisticians [139].

The association was found in adults as well as children, blacks as well as whites, urban as well as rural groups. During the course of the NHANES II study, lead in food in the U.S. has not declined but, if anything, increased (on the basis of market basket studies). This has generally been taken to support the association between petrol lead and blood lead; but it could be argued that if petrol lead exerts as large an influence as was implicated by the NHANES II analyses, at least for adults some part of this influence would be expected to be exerted through the food chain. Adults do not generally show "mouthing activity" and until now, it has not been disputed that at least adults take up most of their lead from food.

The short time lag of 1–2 months suggested between petrol lead consumption changes and blood lead level changes strongly suggests an influence which is mainly direct. This can only mean that either

(1) the influence of air lead on blood lead in adults is greater than has been assumed until now. In view of the experimental evidence, this does not seem very likely.

or (2) there is an as yet unidentified pathway of lead for adults, with short-term fluctuations of lead which closely mirror the fluctuations in petrol lead consumption. In view of the vast body of literature which exists on environmental lead, it will not be easy to suggest a realistic possible pathway that meets these requirements.

The comparable magnitude of the "effect" of petrol lead consumption on blood lead levels in urban and rural groups, and in adults and children is also not easily explained. Curvilinearity of the relationship between lead exposure and blood lead is a possible model for interpretation: smaller changes in exposure, as would be expected in rural vs. urban groups, and in adults vs. children, could theoretically result in more or less equal changes in blood lead, when blood lead levels in urban groups exceed those of rural groups, and blood levels of children exceed those of adults. Both of these last requirements are not unrealistic (cf. ref. 60).

The Turin Isotopic Lead Experiment

The large range of α values calculated from individual studies also raises the question of the contribution of environmental lead to children's blood lead.

Authors like Jones and Stephens [118] have tended to propose an increase in the percentage of lead in children's blood derived from environmental lead pollution, a proposal which has not gone unchallenged [140, 141]. It is thus quite understandable that the progress of the Turin Isotopic Lead Experiment has been watched with increasing attention [41–43]. The

Isotopic Lead Experiment consisted of changing the isotopic composition of lead added to petrol in a large area surrounding Turin, Piedmont, Italy for about 4 years (1975–1979), and to follow the subsequent changes of the isotopic composition of lead in environmental and biological samples of all sorts. Between 1974 and 1981, four phases were discerned in which the average ratio of 206 Pb/207 Pb in petrol sold in the study area were 1.186, 1.111, 1.060 and 1.115, respectively.

In Turin the isotopic ratio of air lead closely followed the ratio of petrol lead, indicating that almost all of the air lead was directly derived from petrol lead. In the surrounding countryside, more lead was shown to be imported from other regions.

Over several years, 1768 blood samples were taken from 458 individuals, mostly members of voluntary blood donor groups and as such not a random sample of the exposed population. Only a few children participated, and (only 5!) preschool children became involved in the project as late as 1980. In adults, blood lead levels were shown to be consistently higher in the countryside than in Turin itself, in smokers as well as non-smokers and in "drinkers" as well as "non-drinkers". There was no explanation for this unusual finding. The number of countryside "non-drinkers" was small, however (less than 10 per area and smoking category), and the "non-drinker" was not exactly defined. Piedmont wines of certified origin had an average lead content of 118 μg/l in 1974–1981 [142]. With the habit of wine consumption integrated in everyday life as it is in Italy, one is tempted to speculate that, if a "non-drinker" is in fact a "light" drinker, relatively minor differences in wine consumption between groups could give rise to the PbB differences that were found. Average levels were high and ranged from 19.8–23.3 μg/100 ml in Turin, from 23.7–28.4 μg/100 ml in the near countryside, and from 25.5–30.8 μg/100 ml in the far countryside, depending on drinking and smoking habits.

In Milan, the other large industrial city of northern Italy, average blood lead levels of 24 to 36 μg/100 ml were found in 4 different population groups in 1971/1972 [143]. It has also been reported that in another, even earlier study, higher PbB values among inhabitants of Milan (34.6 μg/100 ml) than among inhabitants of the surrounding countryside (28.2 μg/100 ml) were found [144].

The 1979 E.C. Blood Lead Survey resulted in 50-percentiles of 14.0 (Milan) and 17.0 μg/100 ml (Turin) for adults [130]. The Isotopic Experiment covered males almost exclusively in Turin, and the Turin E.C. Survey population consisted of almost 60% of females; PbB values were consistently higher in males than in females in the Isotopic Experiment, and as arithmetic means are usually higher than 50-percentiles in PbB distributions due to non-normality, there does not seem to be a wide disagreement between the results of the two different surveys.

Some results of the determinations of the isotopic ratio in blood from the Turin experiment are shown in Table 13 (data from ref. 43).

These results have been interpreted to mean that at least 28% of adult

TABLE 13
$^{206}Pb/^{207}Pb$ RATIO IN BLOOD OF TURIN RESIDENTS

Population group	$^{206}Pb/^{207}Pb$ ratio in blood	$^{206}Pb/^{207}Pb$ ratio in air
Adults, 1975	1.1628	1.174
Adults 1979	1.1325	1.064
Children, 9–10, 1979	1.1249	1.064
Children, 6–12, 1980	1.1189	1.080
Children, 3–5, 1980	1.1119	1.080

blood lead, and 46% of children's blood lead, could be traced to air lead. These figures have been deemed to be underestimates because of the impact of the release of lead with the "original" $^{206}Pb/^{207}Pb$ ratio from bone into the blood, especially in adults, and because of the impact of lead imported into the area in foodstuffs etc., and also originating from air, but in a different area unaffected by the experiment [118]. The experiment has been severely criticized for its selection of study participants [145]. Selection was indeed such that the average impact of air lead on blood lead cannot be derived for random samples from the population. However, the results presented thus far for the different age categories are in close agreement with what could have been expected in terms of age dependency of the $^{206}Pb/^{207}Pb$ ratios.

The lead content of petrol, the lead emission per surface unit and the lead concentrations in air were all rather high in the study area, which would suggest that a larger influence of petrol lead on blood lead can be expected in this area than in other cities of comparable magnitude, but with different petrol lead contents and traffic flow patterns. On the other hand, PbB levels were high too, especially in the countryside, which in its turn would tend to diminish the percentual influence of petrol lead on blood lead.

CONCLUSIONS

It is not possible, on the basis of published studies, to make a reliable quantitative estimate of the relationship between air lead and children's blood lead. Unlike adults, who are mainly exposed to environmental lead through inhalation of polluted air, children take up lead from the environment through a variety of pathways, and it seems probable that the large range of α values which can be derived from the literature at least in part reflects differences in living circumstances, access to other pathways, play habits, etc., which all serve to modify the relationship between air lead as an indicator of environmental pollution on the one hand, and children's blood lead as an indicator of lead actually taken up from the environment on the other.

The use of multiple indicators of lead pollution is advisable, and in case of doubt biological monitoring of children's blood lead remains the only reliable method for determining actual health risks. The large range of α values presented here is at variance with most published reviews on the subject, which have tended to conclude that α for children is not much larger than it is for adults. For at least a number of child populations investigated, this seems to be incorrect. This is not to imply that in general, small increases of the air lead concentration will produce large increases of children's blood lead. In urban situations with traffic as the main lead source, and without excessive additional lead uptake through paint or drinking water, children's blood lead levels have usually not been exceptionally high.

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APPENDIX I

AIR LEAD AND BLOOD LEAD IN 96 DIFFERENT CHILD POPULATIONS FROM 18 DIFFERENT STUDY AREAS

Reference	PbA ($\mu g/m^3$)	PbB (μg/100 ml)	Comment
8	0.40	18.0	
	0.69	22.0	cf. Review section
	0.83	24.0	
99	0.50	11.3	
	2.50	15.2	
77	2.50	19.7	
	0.50	11.8	
76	0.50	14.6	
	1.50	18.2	
78	0.40	16.6	
100	0.40	13.1	
	0.20	8.2	
67	2.90	16.1	
	0.50	7.0	
68–71	5.60	40.4	
	1.10	7.8	
112, 113	0.50	7.6	
	0.10	5.0	
105, 106	6.30	20.8	Boys
		14.9	Girls
	0.60	10.4	Boys
		9.6	Girls
17	0.67	12.9	Boys
		9.6	Girls
	0.89	16.5	Boys
		18.6	Girls
	1.07	11.7	Boys
		14.9	Girls
	1.54	15.1	Boys
		13.6	Girls
37, 48	10.00	41.4	
	6.00	31.2	
	3.00	20.2	

(continued)

APPENDIX I (*continued*)

Reference	PbA (μg/m³)	PbB (μg/100 ml)	Comment
82	23.80	46.3	
		44.4	
		45.9	
		46.8	
	0.30	7.0	
38	20.80	46.7	
		49.2	
	0.10	10.3	
		10.6	
83,84	3.30	28.0	
	0.90	19.0	
85–87	4.06	30.1	
	1.00	21.1	
	0.29	9.4	
	2.94	26.4	
	0.74	13.6	
	0.31	9.1	
	3.67	24.6	
	0.80	13.3	
	0.45	10.4	
	0.30	9.0	
	3.42	28.9	
	0.49	14.8	
	2.68	27.8	
	0.54	16.0	
	0.56	12.7	
	0.37	10.7	
88, 89	2.00	22.0	
	0.50	11.0	
90	1.60	31.6	Girls
		38.7	Boys
	0.50	19.1	Girls
		21.0	Boys
40, 91, 92, 94	16.50	76.0	Data as mentioned in [94], only data from 1974 were used, cf. Review section. Of these, only 4- and 8-year olds, to prevent too large an influence upon the analysis of data from one single study
		61.0	
	14.20	47.0	
		43.0	
	6.70	36.0	
		32.0	
	2.80	33.0	
		33.0	
	0.70	30.0	
		28.0	
	0.50	23.0	
		23.0	

APPENDIX I (*continued*)

Reference	PbA (μg/m³)	PbB (μg/100 ml)	Comment
59, 72, 73	2.90	28.5	Air lead values calculated from figure in [59], and corrected for measuring height; PbB data for 37–48 month olds only, to prevent too large an influence upon the analysis of data from one single study
		25.0	
		26.5	
	2.10	29.8	
		24.8	
		23.0	
	1.90	25.8	
		22.6	
		21.0	
	1.60	25.8	
		23.3	
		22.2	
	1.60	24.5	
		22.8	
		21.6	
	1.40	22.4	
		20.9	
		18.0	